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Published:
— *with international search report*
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: FUNCTIONAL INACTIVATION OF CXCR4-MEDIATED RESPONSES IN GROWTH HORMONE TRANSGENIC MICE THROUGH SOCS3 UPREGULATION

(57) Abstract: The present invention permits data, derived from bGH-Tg mice in the context of crosstalk between cytokine and chemokine responses, to aid in understanding the functional role of this chemokine/chemokine receptor pair. As the only models available to date were thoses in which the CXCR4 or CXCL12 deletion is lethal before birth the present invention provides means for relating cytokine-mediated effects to the functional role of CXCR4 inactivation in postanatal life. A method is provided for treating a human having a disease associated with CXCR4-dependent HIV comprising administering to said human a therapeutically anti-viral effective amount of a molecule that induces the expression of SOCS3 and a pharmaceutically acceptable carrier. A method is provided for treating a human having a disease associated with CXCR4-dependent HIV, wherein said molecule binds to GHR.

INTERNATIONAL SEARCH REPORT

Interna[illegible]lication No
PCT/IB 02/05789

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/50 G01N33/74 G01N33/68 G01N33/569

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
MEDLINE, EMBASE, BIOSIS, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; March 1998 (1998-03) LEISSNER P ET AL: "In vitro and in vivo inhibition of HIV-1 replication by retroviral transfer of TAT-inducible interferon alpha, beta or gamma genes: Application to gene therapy for AIDS" Database accession no. PREV199800302718 XP002259515 abstract & ANNALES DE BIOLOGIE CLINIQUE, vol. 56, no. 2, March 1998 (1998-03), pages 167-173, ISSN: 0003-3898 --- -/--	10,11

[X] Further documents are listed in the continuation of box C. [ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 October 2003	20/11/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Luis Alves, D

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CALIGIURI M A ET AL: "Selective modulation of human natural killer cells in vivo after prolonge infusion of low dose recombinant interleukin 2" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 93, no. 19, 17 September 1996 (1996-09-17), pages 10405-10410, XP002155131 ISSN: 0027-8424 abstract --- SORIANO SILVIA F ET AL: "Functional inactivation of CXC chemokine receptor 4-mediated responses through SOCS3 up-regulation." THE JOURNAL OF EXPERIMENTAL MEDICINE. UNITED STATES 5 AUG 2002, vol. 196, no. 3, 5 August 2002 (2002-08-05), pages 311-321, XP002259351 ISSN: 0022-1007 the whole document --- VILA-CORO A J ET AL: "The chemokine SDF-1'alpha! triggers CXCR4 receptor dimerization and activates the JAK/STAT pathway" FASEB JOURNAL 1999 UNITED STATES, vol. 13, no. 13, 1999, pages 1699-1710, XP002259352 ISSN: 0892-6638 cited in the application abstract --- AUERNHAMMER C J ET AL: "The central role of SOCS-3 in integrating the neuro-immunoendocrine interface" JOURNAL OF CLINICAL INVESTIGATION 2001 UNITED STATES, vol. 108, no. 12, 2001, pages 1735-1740, XP002259353 ISSN: 0021-9738 the whole document --- -/--	10,11 1-12 1-12 1-12

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HESSELGESSER J ET AL: "Identification and characterization of the CXCR4 chemokine receptor in human T cell lines: ligand binding, biological activity, and HIV-1 infectivity." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 15 JAN 1998, vol. 160, no. 2, 15 January 1998 (1998-01-15), pages 877-883, XP002259354 ISSN: 0022-1767 abstract	1-12
A	KREBS DANIELLE L ET AL: "SOCS proteins: Negative regulators of cytokine signaling" STEM CELLS (MIAMISBURG), vol. 19, no. 5, 2001, pages 378-387, XP002259355 ISSN: 1066-5099 the whole document	1-12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/05789

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10 to 12 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.